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REMARKS

Status of the claims

Claims 1 and 9 are currently amended. Claims 1, 3-17 are pending and under consideration.

Priority

The Office has established an earliest priority date of March 16, 1999, and has not granted the earlier filing date of March 26, 1998 because Applicants had not filed a certified English language translation of foreign priority document DE 198 13 317.0. The Office has acknowledged receipt of a certified copy of this German application.

In accordance with 37 CFR 1.55 and MPEP §201.15, to perfect the claim to the foreign priority date of the German application 198 13 317.0 filed on March 26, 1998, Applicants file herewith a certified English language translation together with a statement from the translator declaring that the English language document is a true and accurate translation of the German application.

Accordingly, Applicants request that the earliest priority date be acknowledged as March 26, 1998.

Claim Rejection - 35 USC § 102

The Office has rejected claims 1, 3, 5-11 and 13-17 under 35 U.S.C. 102(a) as being anticipated by Dietmaier et al. (Action page 3). Applicants respectfully traverse the rejection.

As discussed in the *Priority* section, above, Applicants have provided an English language translation together with a statement from the translator declaring the accuracy of the translation, thereby perfecting the claim to the foreign priority date. The Dietmaier et al. reference was published in January, 1999; the foreign priority date for the present application is March 26, 1998 which predates the publication date of the Dietmaier reference.

Therefore, Applicants respectfully request withdrawal of the 102(a) rejections.

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Claim Rejection - 35 USC § 103

The Office has rejected claims 1 and 3-17 under 35 U.S.C 103(a) as being unpatentable over Eggeling et al. in view of Biochemicals Catalog (Action page 6). Applicants respectfully traverse the rejection.

Applicants respectfully submit that the Office has failed to demonstrate any motivation or suggestion in the art at the time the invention was made to combine the teachings of Eggeling and the Biochemicals Catalog in the asserted manner. MPEP \$706.02(j). Without such a demonstration, no *prima facie* case of obviousness can be established.

Applicants assert that the person of ordinary skill in the art would not have been motivated to use the ExpandTM High Fidelity enzyme blend as described in the Biochemicals Catalog, the ExpandTM enzyme blend is a mixture of Taq polymerase and Pwo polymerase for the amplification of nucleic acid fragments up to 6 kb. The Pwo polymerase has 3'-5' proofreading activity that increases the fidelity of the amplification system, resulting in a reduced error rate. Additionally, the ExpandTM enzyme blend enhances amplification by reducing secondary structures. Eggeling describes a method for amplification using two amplification reactions containing the single enzyme Taq polymerase, which does not have 3'-5' proofreading activity. The Office has failed to demonstrate that fidelity of the amplification or error rate was an issue in practicing the method of Eggeling, or that secondary structures were of concern in Eggeling. The Office has failed to demonstrate that that there were experimental limitations in the method of Eggeling that would motivate one skilled in the art to increase the fidelity of the amplification or reduce the effects of secondary structure by the addition of 3'-5' proofreading activity.

Applicants herewith present a Declaration by Dr. Gregor Sagner, Ph.D., Director of R&D with Roche Applied Sciences, Penzberg, Germany ("Declaration"). Dr. Sagner is not named as an inventor on this application, nor does he have any legal interest in this application. Dr. Sagner asserts that it would not have been obvious to substitute the ExpandTM system in the method of Eggeling et al., because the ExpandTM system, as can be deduced from the catalog, is intended to be used for the amplification of long (>1000 bp) templates ("...and the ExpandTM PCR System's unique blend of thermostable enzymes lead to greater fidelity (low error rate) and larger fragments (up to 6 kb)". Dr. Sagner explains

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that at the time the invention was made, it was known in the art that amplification of PCR fragments of about 550 bp or smaller could be generated with almost 100% fidelity, such that no 3'-5' proofreading activity was required. Therefore, one of skill in the art would be concerned about increased fidelity, and the beneficial effects of 3'-5' proofreading activity thereon, only when amplification of PCR fragments greater than about 500 bp was desired.

Dr. Sagner also explains that the method of Eggeling et al. uses Taq DNA polymerase for both random and specific amplification steps. Eggeling et al. discloses the generation of 0.2-0.5 amplification products for the first round of amplification, i.e. the whole genome amplification with random primers. For the second round of specific amplification, they disclose amplification of microsatellite loci without mentioning the size (these loci are typically below 100 bp) and amplification of the ameliogenin gene resulting in amplification products of about 106/112 bp in size. Consequently, Dr. Sagner concludes that there would be no motivation to replace the Taq polymerase with an enzyme mixture comprising a DNA polymerase with 3'-5' proofreading activity, simply because there is no reason why one of skill in the art would believe that such an activity might increase the performance of the method disclosed by Eggeling et al.

Applicants have amended claims 1 and 9 to recite the limitation of "fragments between 100 and 550 base pairs in length". Applicants assert that in such "small template" amplification, where fidelity was not of concern to those skilled in the art, there was no motivation in Eggeling et al. to use a mixture of enzymes comprising 3'-5' proofreading activity. In fact, because substitution for Taq DNA polymerase with the ExpandTM enzyme mixture described in the Biochemicals Catalog would have conferred no benefit in the practice of the method of Eggeling et al., the prior art would have tended to teach away from such a substitution.

Thus, because the Office has not established a prima facie case of obviousness, Applicants respectfully request reconsideration and withdrawal of the §103 rejections.

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CONCLUSION

Applicants respectfully assert that the present application is in condition for allowance and request that the Office issue a timely Notice of Allowance.

Under 37 CFR §1.136(a), Applicants respectfully request a 3-month extension of time to respond to the Office Action mailed May 17, 2005. The response date was August 17, 2005; with the granting of this request, the response time is re-set to November 17, 2005. The commissioner is hereby authorized to charge the amount of \$1020, the fee due under 37 CFR §1.17(a)(3), to Deposit Account No. 50-0812. Please grant any other extensions of time required to enter this amendment and charge any additional fees or credit any overpayments to Deposit Account No. 50-0812.

Please direct all future correspondence to: Customer No. 22829.

Respectfully submitted,

Date: November 16, 2005

Rhea C. Nersesian Reg. No. 55,488

Correspondence Address
Roche Molecular Systems, Inc.
1145 Atlantic Avenue
Alameda, California 94501
Tele: 510-814-2800

Fax: 510-814-2973